

In the Claims:

Please amend Claims 1, 13, 25, 26, 39, 52, 64, 76, 80, 82 and 84 as shown in the following clean replacement claims. A marked up copy of the amended Claims is attached as Attachment 2.

In the Claims, please delete Claims 1, 11-13, 23-25, 26, 37-39, 50-52, 62-64, 74-76, 80, 82, and 84 and substitute therefor the following amended claims.

1. (amended) A method for enhancing the solubility of, and promoting the adoption of native folding conformation, of a protein or polypeptide expressed by recombinant DNA techniques in a host cell, the method comprising:

- a) providing a first nucleic acid sequence encoding a protein or polypeptide of interest, the protein or polypeptide being substantially insoluble, or biologically inactive, when expressed in a host cell by recombinant DNA techniques;
- b) providing a second nucleic acid sequence encoding a peptide extension having a net negative charge, the peptide T7A (SEQ ID NO: 20) of Table 1 being specifically excluded;
- c) fusing the second nucleic acid sequence to the first nucleic acid sequence in an expression vector such that a fusion protein encoded by the first and second nucleic acid sequences is expressed in the host cell following transformation of the host cell with the expression vector encoding the fusion protein, the peptide extension encoded by the second nucleic acid sequence being positioned at the carboxyl-terminus of the protein or polypeptide of interest;

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- d) transforming the host cell with the expression vector encoding the fusion protein; and
  - e) culturing the transformed host cells under conditions appropriate for the expression of the fusion protein.

13. (Amended) The method of Claim 11, wherein the peptide extension is selected from the group consisting of: Peptide T7C (SEQ ID NO: 5), Peptide T7B (SEQ ID NO: 6), Peptide T7B1 (SEQ ID NO: 7), Peptide T7B2 (SEQ ID NO: 8), Peptide T7B3 (SEQ ID NO: 9), Peptide T7B5 (SEQ ID NO: 11), Peptide T7B6 (SEQ ID NO: 12), Peptide T7B7 (SEQ ID NO: 13), Peptide T7B8 (SEQ ID NO: 14), Peptide T7B9 (SEQ ID NO: 15), Peptide T7B10 (SEQ ID NO: 16), Peptide T7B11 (SEQ ID NO: 17), Peptide T7B12 (SEQ ID NO: 18), Peptide T7B13 (SEQ ID NO: 19), Peptide T7A1 (SEQ ID NO: 21), Peptide T7A2 (SEQ ID NO: 22), Peptide T7A3 (SEQ ID NO: 23), Peptide T7A4 (SEQ ID NO: 24) and Peptide T7A5 (SEQ ID NO: 25).

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25. (amended) The method of Claim 23, wherein the peptide extension is selected from the group consisting of: Peptide N1 (SEQ ID NO: 27), Peptide N2 (SEQ ID NO: 28), Peptide N3 (SEQ ID NO: 29), Peptide N4 (SEQ ID NO: 30), Peptide N5 (SEQ ID NO: 31), Peptide N6 (SEQ ID NO: 32) and Peptide N7 (SEQ ID NO: 33).

26. (amended) A method for enhancing the *in vitro* renaturation of a protein or polypeptide expressed by recombinant DNA techniques in a host cell, a substantial percentage of the expressed protein or polypeptide being localized in inclusion bodies following expression in the host cell, the method comprising:

- a) providing a first nucleic acid sequence encoding a protein or polypeptide of interest;
- b) providing a second nucleic acid sequence encoding a peptide extension having a net negative charge, the peptide T7A (SEQ ID NO: 20) of Table 1 being specifically excluded;
- c) fusing the second nucleic acid sequence to the first nucleic acid sequence in an expression vector such that a fusion protein encoded by the first and second nucleic acid sequences is expressed in a host cell following transformation of the host cell with the expression vector encoding the fusion protein, the peptide extension encoded by the second nucleic acid sequence being positioned at the carboxyl-terminus of the protein or polypeptide of interest;
- d) transforming the host cell with the expression vector encoding the fusion protein, under conditions appropriate for expression of the fusion protein;
- e) isolating inclusion bodies from lysates of the host cell;
- f) contacting the isolated inclusion bodies with a denaturing solution thereby solubilizing the fusion protein comprising the inclusion body;

and,

- g) suspending the solubilized fusion protein of step f) in a renaturation buffer.

39. (Amended) The method of Claim 37, wherein the peptide extension is selected from the group consisting of: Peptide T7C (SEQ ID NO: 5), Peptide T7B (SEQ ID NO: 6), Peptide T7B1 (SEQ ID NO: 7), Peptide T7B2 (SEQ ID NO: 8), Peptide T7B3 (SEQ ID NO: 9), Peptide T7B5 (SEQ ID NO: 11), Peptide T7B6 (SEQ ID NO: 12), Peptide T7B7 (SEQ ID NO: 13), Peptide T7B8 (SEQ ID NO: 14), Peptide T7B9 (SEQ ID NO: 15), Peptide T7B10 (SEQ ID NO: 16), Peptide T7B11 (SEQ ID NO: 17), Peptide T7B12 (SEQ ID NO: 18), Peptide T7B13 (SEQ ID NO: 19), Peptide T7A1 (SEQ ID NO: 21), Peptide T7A2 (SEQ ID NO: 22), Peptide T7A3 (SEQ ID NO: 23), Peptide T7A4 (SEQ ID NO: 24) and Peptide T7A5 (SEQ ID NO: 25).

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52. (Amended) The method of Claim 50, wherein the peptide extension is selected from the group consisting of: Peptide N1 (SEQ ID NO: 27), Peptide N2 (SEQ ID NO: 28), Peptide N3 (SEQ ID NO: 29), Peptide N4 (SEQ ID NO: 30), Peptide N5 (SEQ ID NO: 31), Peptide N6 (SEQ ID NO: 32) and Peptide N7 (SEQ ID NO: 33).

64. (Amended) The expression vector of Claim 62, wherein the peptide extension is selected from the group consisting of: Peptide T7C (SEQ ID NO: 5), Peptide T7B (SEQ ID NO: 6), Peptide T7B1 (SEQ ID NO: 7), Peptide T7B2 (SEQ ID NO: 8), Peptide T7B3 (SEQ ID NO: 9), Peptide T7B5 (SEQ ID NO: 11), Peptide T7B6 (SEQ ID NO: 12), Peptide T7B7 (SEQ ID NO: 13), Peptide

10 T7B8 (SEQ ID NO: 14), Peptide T7B9 (SEQ ID NO: 15), Peptide T7B10  
(SEQ ID NO: 16), Peptide T7B11 (SEQ ID NO: 17), Peptide T7B12 (SEQ  
ID NO: 18), Peptide T7B13 (SEQ ID NO: 19), Peptide T7A1 (SEQ ID NO:  
21), Peptide T7A2 (SEQ ID NO: 22), Peptide T7A3 (SEQ ID NO: 23),  
Peptide T7A4 (SEQ ID NO: 24) and Peptide T7A5 (SEQ ID NO: 25).

76. (Amended) The expression vector of Claim 74, wherein the peptide extension is  
selected from the group consisting of: Peptide N1 (SEQ ID NO: 27), Peptide  
N2 (SEQ ID NO: 28), Peptide N3 (SEQ ID NO: 29), Peptide N4 (SEQ ID  
NO: 30), Peptide N5 (SEQ ID NO: 31), Peptide N6 (SEQ ID NO: 32) and  
Peptide N7 (SEQ ID NO: 33).

80. (Amended) A method for enhancing the solubility of, and promoting the adoption  
of native folding conformation, of a protein or polypeptide expressed by  
recombinant DNA techniques in a prokaryotic cell, the method comprising:  
a) providing a first nucleic acid sequence encoding a protein or  
polypeptide of interest, the protein or polypeptide being substantially  
insoluble, or biologically inactive, when expressed in a prokaryotic  
cell by recombinant DNA techniques;  
b) providing a second nucleic acid sequence encoding a peptide  
extension having a net negative charge, the peptide T7A (SEQ ID  
10 NO: 20) of Table 1 being specifically excluded;  
c) fusing the second nucleic acid sequence to the first nucleic acid  
sequence in a prokaryotic expression vector such that a fusion protein  
encoded by the first and second nucleic acid sequences is expressed in

a prokaryotic cell following transformation of the prokaryotic cell with the prokaryotic expression vector encoding the fusion protein, the peptide extension encoded by the second nucleic acid sequence being positioned at the carboxyl-terminus of the protein or polypeptide of interest;

- d) transforming the prokaryotic cell with the prokaryotic expression vector encoding the fusion protein; and
- e) culturing the transformed prokaryotic cells under conditions appropriate for the expression of the fusion protein.

82. (Amended) A method for enhancing the *in vitro* renaturation of a protein or polypeptide expressed by recombinant DNA techniques in a prokaryotic cell, a substantial percentage of the expressed protein or polypeptide being localized in inclusion bodies following expression in the prokaryotic cell, the method comprising:

- a) providing a first nucleic acid sequence encoding a protein or polypeptide of interest;
- b) providing a second nucleic acid sequence encoding a peptide extension having a net negative charge, the peptide T7A (SEQ ID NO: 20) of Table 1 being specifically excluded;
- c) fusing the second nucleic acid sequence to the first nucleic acid sequence in a prokaryotic expression vector such that a fusion protein encoded by the first and second nucleic acid sequences is expressed in a prokaryotic cell following transformation of the prokaryotic cell

with the prokaryotic expression vector encoding the fusion protein,  
the peptide extension encoded by the second nucleic acid sequence  
being positioned at the carboxyl-terminus of the protein or  
polypeptide of interest;

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- d) transforming the prokaryotic cell with the prokaryotic expression  
vector encoding the fusion protein, under conditions appropriate for  
expression of the fusion protein;
- e) isolating inclusion bodies from lysates of the prokaryotic cell;
- f) contacting the isolated inclusion bodies with a denaturing solution  
thereby solubilizing the fusion protein comprising the inclusion body;  
and,
- g) suspending the solubilized fusion protein of step f) in a renaturation  
buffer.

84. (Amended) An antibody which binds specifically to one or more polypeptides  
selected from the group consisting of: Peptide T7C (SEQ ID NO: 5), Peptide  
T7B (SEQ ID NO: 6), Peptide T7B1 (SEQ ID NO: 7), Peptide T7B2 (SEQ  
ID NO: 8), Peptide T7B3 (SEQ ID NO: 9), Peptide T7B5 (SEQ ID NO: 11),  
Peptide T7B6 (SEQ ID NO: 12), Peptide T7B7 (SEQ ID NO: 13), Peptide  
T7B8 (SEQ ID NO: 14), Peptide T7B9 (SEQ ID NO: 15), Peptide T7B10  
(SEQ ID NO: 16), Peptide T7B11 (SEQ ID NO: 17), Peptide T7B12 (SEQ  
ID NO: 18), Peptide T7B13 (SEQ ID NO: 19), Peptide T7A1 (SEQ ID NO:  
21), Peptide T7A2 (SEQ ID NO: 22), Peptide T7A3 (SEQ ID NO: 23),  
Peptide T7A4 (SEQ ID NO: 24) and Peptide T7A5 (SEQ ID NO: 25),

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